REMARKS AND ARGUMENTS

I. AMENDMENTS TO THE SPECIFICATION

Removal of hyperlink

Applicants have herein amended the specification to comply with the Examiner's request to remove embedded hyperlinks (MPEP § 608.01).

II. CLAIM AMENDMENTS

The Applicants assert that these amendments add no new matter and their incorporation is respectfully requested. Please cancel claims 1-6 and 14-16 without prejudice or disclaimer. Claims 7-9 and 11-13 have been amended to better point out and describe the invention and to correct dependency. Support for the claim amendments are at least as follows;

Claim 7 at least at Figure 102.

Claim 8-9 have been amended to correct dependency.

Claim 11 at least at Figure 101.

Claim 12-13 have been amended to correct dependency.

Claim 17 have been amended to correct dependency.

III REJECTIONS

A. The Rejection under 35 U.S.C. § 101/§ 112.

Claims 1-20 stand rejected under 35 U.S.C. § 101 as allegedly not being supported by either a specific and substantial asserted or a well-established utility. The general basis of the Examiner's rejection is that the data presented in Example 18 of the present specification is insufficient to establish a patentable utility for the presently claimed subject matter. Applicants respectfully traverse the rejection.

The Legal Standard

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in Brenner v. Manson, 383 U.S. 519, 534 (1966) stating that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. § 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to

satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "'substantial'" utility.'" (M.P.E.P. § 2107.01, emphasis added). Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, § 2107 II(B)(1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility".

The PTO also sets forth the evidentiary standard as to utility rejections. In general, an Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. § 101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974). See, also In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); In re Irons, 340 F.2d 974, 144 USPQ 351 (1965); In re Sichert, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977). Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. Only after the Examiner makes a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift back to the applicant.

The Data At Issue

In support of the outstanding utility rejection, the Examiner maintains the §101/§112 rejection citing Haynes et al., (Haynes P.A. et al., Electrophoresis 19:1862-1871 (1998)), Hu et al., Wang et al., and has cited further art from Anderson et al. The Examiner uses these references to reject the Applicants assertion that it is more likely than not for increased mRNA expression to result in increased protein levels. Applicants cite Mijalski et al., and Mootha et al., as more relevant and recent art than that cited by the Examiner ((Mijalski et al., PNAS 102(24):86921-26(2005), (Mootha et al, Cell 115:629-640 (2003)). Mijalski used DNA microarray expression profiling combined with 2D gels and peptide mass fingerprinting to compare the mRNA levels of the transcriptome with the protein levels of the proteome. Using this approach Mijalski used > 20,200 probes which identified > 1,800 transcripts that were differentially regulated with statistical significance in mouse liver and kidney. The protein analysis covered about 2,300 gel spots for each organ. Mijalski uses this data to compare the levels of gene expression with the levels of protein expression and finds that they are reasonably correlated. From his

discussion section on page 8626, left column, Mijalski states; "This observation suggests that, at least for the most differential proteins, gene expression at the transcript level correlates well with protein expression." To refine this analysis, Mijalski looked at transcriptional versus translational regulation of 37 proteins and found that 78.4% had protein levels that correlated with the mRNA levels, 13.5% were not differentially expressed and only 5.4% had the opposite tendency to be regulated at the protein level, rather than the RNA level. This is shown graphically in Figure 4 of Mijalski.

In a paper by Mootha et al., they used mass-spectrometry based proteomics to profile mitochondrial protein composition across 4 different tissues, and then subject this data to a concordance test designed to eliminate technical artifacts or "noise" in the data (Mootha et al, Cell 115:629-640 (2003)). The algorithm and logic that Mootha have used to design the concordance test is given in the Experimental procedures section of the paper on page 638. The concordant analysis was applied to proteins identified in well-matched brain, heart, kidney and liver for which Mootha also had mRNA expression measured. Mootha found that 426 out of 569 comparisons passed the concordance test and allowed them to conclude on page 633; "We found that 426 of the 569 pairwise comparisons were concordant, allowing us to strongly reject the null hypothesis that there is no association between protein detection and mRNA abundance ($p=3.0 \times 10^{-14}$). Hence, on a bulk level, mRNA expression levels are indeed correlated to detection by proteomics."

The Applicants have also included a declaration by Dr. Paul Polakis, which states that in general there is a correlation between mRNA levels and polypeptide levels. Dr. Polakis states that the primary focus of his work is to identify tumor cell markers useful as targets for both the treatment and the diagnosis of cancer in humans. His lab relies on the results of microarray experiments in their efforts to identify such markers. Using microarray analysis, Genentech scientists have identified about 200 genes that are present in human tumors at higher levels than corresponding non-tumor tissue or cells. As of the date of the declaration, approximately 30 antibodies have been generated that bind to polypeptides identified as overexpressed by microarray analysis. These antibodies have been used to quantitatively determine the level of production of the identified proteins in the tumors and normal tissue. In approximately 80% of their experiments, they have found that increases in the level of mRNA correlates with changes in the level of the corresponding protein.

Applicants have submitted articles from respected journals that support conclusions made by the Applicants that mRNA levels correlate with protein expression. Applicants have also submitted a declaration from a scientist who has reviewed the data and asserted that in general, there is a correlation between mRNA expression and protein expression. The data by Mijalski that the genes examined in their

study had a 78.4% correlation between mRNA and protein level and by Mootha that their data had high statistical significance ($p=3.0 \times 10^{-14}$) between mRNA and protein level supports the Applicant's assertion that it is more likely than not that increased mRNA expression leads to increased protein levels. Therefore it is more likely than not that the melanoma data provided by the Applicants on PRO3579 nucleic acid is a useful and substantial utility, and in light of these facts and the amendments to the claims, Applicants respectfully request reconsideration and withdrawal of the outstanding rejection.

B. The Rejection under 35 U.S.C. § 112 first paragraph

The Examiner has rejected Claims 1-20 under 35 U.S.C § 112 first paragraph as allegedly not complying with the enablement requirement. The Examiner has rejected the claims citing lack or direction for one skilled in the art to practice DNA68862-2546 polynucleotides encoding PRO3579 polypeptides that are not identical to the sequences disclosed in SEQ ID NO: 101 and SEQ ID NO: 102.

Applicants have amended the claims to comply with the Examiner's suggestion and thus withdrawal of this rejection is respectfully requested.

C. The Rejection under 35 U.S.C. § 102(f)

The Examiner has maintained the rejection of Claims 1-17 under 35 U.S.C. 102(f) as the inventors have allegedly derived the subject matter claimed. In support of this rejection the Examiner has cited Applicant's U.S. provisional application 60/170,262, which states Applicants purchased a EST from Incyte Corporation and the cDNA insert was obtained and sequenced. Applicants respectfully traverse the rejection.

The issue of derivation under 35 U.S.C. 102(f) is one of fact and the party asserting derivation has the burden of proof. Derivation is shown by two prongs.

1. A prior, complete conception of the claimed subject matter; and
2. a communication of the complete conception to the party charged with derivation. (Kilbey v. Thiele, 199 USPQ 294).

Prior, complete conception of the claimed subject matter.

A conception must include all of the essential features of the invention. (Cislak v. Wagner 215 F.2d 275, 103 USPQ 39.) Cislak was a case in front of the Board of Interference Examiners of the United States Patent Office in which the single count in interference related to the production of vinyl pyridine by dehydrogenation of ethyl pyridine. It was apparent from the notebooks of Cislak and his assistant that they had discussed producing vinyl pyridine from ethyl pyridine, but the board was not persuaded that the

evidence indicated that Cislak had sufficient conception of the invention. The Board's decision which was upheld on appeal stated "It is not sufficient that Cislak had a general idea that vinyl pyridine could be produced from ethyl pyridine by catalytic dehydrogenation. Conception must include all the essential features of the invention of the count, and must be manifested or proved by exterior acts or disclosures." Applicants assert that the essential features of their invention are; 1) a nucleic acid sequence, 2) the polypeptide encoded by the disclosed nucleic acid sequence and fragments thereof, and 3) that the nucleic acid is overexpressed in melanoma. The Incyte EST 2377329 as cited by the Examiner, is a nucleic acid sequence, but it does not include all of the essential features of the invention. It does not disclose an encoded protein, nor the melanoma data. The Examiner concedes that "the only arguable contribution that the Applicants make is the identification of the nucleotide sequence of SEQ ID NO: 101 and the characterization of its coding sequence." Indeed, this is precisely the essential element of any isolated gene/polypeptide invention. The partial sequence of the Incyte EST 2377329 does not provide this and thus does not disclose all the essential features of the invention. Therefore, under Cislak, the Incyte EST 2377329 cannot be considered as prior art under 35 U.S.C. 102(f).

For 35 U.S.C. 102(f) to be effective it must read on the claimed subject matter. Applicants claim amendments have rendered Incyte EST 2377329 ineffective as an available reference under 35 U.S.C. 102(f). Incyte EST 2377329 is identical to nucleotides 1-197 of SEQ ID NO: 101 (See Exhibit A). Applicants claim amendments have claimed nucleotides 200 and greater, therefore Incyte EST 2377329 does not read on any of the amended claims. Thus Incyte EST 2377329 is outside of the 35 U.S.C. 102(f) requirement of claimed subject matter, and cannot be considered prior art.

Communication of the complete conception to the party charged with derivation.

The second requirement under 35 U.S.C. 102(f) is that communication of complete conception must be sufficient to enable one of ordinary skill in the art to construct and successfully operate the invention. Proof of motive and opportunity such as access is not sufficient to prove derivation. (Hedgewick v. Akers 497 F.2d at 908, 182 USPQ 167). In Hedgewick, the dispute was over a container which employed a safety cap. Akers had experience in the area of plastic closures and safety caps, and had been hired by Hedgewick. When Akers left for another employer in which he conceived a safety cap very similar to the Hedgewick cap, Hedgewick alleged that Akers had used information obtained during his employment to create his invention. The decision of the Board and court held that Hedgewick had failed to meet his burden of proof for derivation as allowing Akers access to the engineering files without more, is insufficient to establish derivation (Hedgewick supra, 169). Applicants submit that the facts of the instant case are similar to that of Hedgewick. Applicants have paid for access to the Incyte database

containing 1,000s of ESTs. The Applicants submit that having database access is much like Akers having access to the engineering files, and is not communication of complete conception of the invention and it may not even qualify as "communication" under Hedgewick. This is insufficient to establish derivation.

Assuming arguendo, that communication did occur, the requirement of complete conception did not. In arriving at conception the inventor may confer and adopt ideas and materials derived from many sources, as long as the inventor maintains intellectual domination of the work of making the invention down to the successful testing, selecting or rejecting as he goes, and does not lose his quality as inventor as having received a suggestion or material from another even if such suggestion proves to be the key that unlocks his problem (Morse v. Porter 155 USPQ 283). Morse was a sales development engineer in the production and sales of sanitary napkins. He consulted with several people on fabrics and knitting production in the development of a napkin that would mold to the body. The Board held that Morse qualified as the inventor of the napkin, as the consultants were simply supplying him with materials or examples of knitting. The properties that made the napkin patentable were controlled by Morse with the consultants not being aware of the napkin problem. Applicants assert that at best, Incyte can be considered a consultant who supplied Applicants with materials, with no knowledge of the complete conception of the invention by the Applicants.

Applicants submit that the Examiner has not fulfilled his burden of proof in proving either of the two prongs of a prior complete conception of the claimed subject matter and communication of that subject matter as required by Kilbey. Also, the current amendments to the claims insure that no claim reads on the cited art, and respectfully request that this rejection be withdrawn.

D. The Rejection under 35 U.S.C. § 112 first paragraph

The Examiner has rejected Claims 1-9, 11-20 under 35 U.S.C. §112 first paragraph as allegedly failing to comply with the written description requirement. The Examiner has objected to the limitation in the claims of nucleic acid sequence encoding polypeptides having acyltransferase activity. Applicants have canceled Claims 1-6 and Claim 14 which contained the acyltransferase activity limitation. The claims as currently amended do not recite nucleic acid sequences encoding polypeptides having acyltransferase activity and withdrawal of this rejection is respectfully requested.

E. The Rejection under 35 U.S.C. § 112 first paragraph

The Examiner has rejected Claims 1-6, 9, 14 and 20 under 35 U.S.C. §112 first paragraph as allegedly failing to comply with the written description requirement. The Examiner has rejected the Applicants claiming amino acids 109-353 of SEQ ID NO:102, and has read into the claim this implies this region is an extracellular or intracellular domain, and as such requires that the membrane topology of

the polypeptide be disclosed. Applicants respectfully traverse the rejection. Applicants have canceled Claims 1-6 and 14-16, and changed the dependency of Claims 17-20, thus leaving Claim 9 at issue. Applicants have disclosed 3 transmembrane domains in Figure 102 of the specification, and amino acids 109-353 are located between two of the transmembrane domains. Applicants submit that they may claim smaller sections of a disclosed protein without violating the requirements of §112 first paragraph and Applicants respectfully request that this rejection be withdrawn.

SUMMARY

In view of the above amendments and remarks, the subject application is believed to be in good and proper order for allowance. Early notification to this effect is earnestly solicited.

Should the Examiner not agree that all claims are allowable, then a personal or telephonic interview is respectfully invited to discuss any remaining issues and accelerate the eventual allowance of this application.

No fee is believed to be due for the submission of this response. Should any fees be required, however, please charge such fees to Genentech, Inc.'s Deposit Account No. 07-0630.

Respectfully submitted,
GENENTECH, INC.

Date: August 10, 2005 By: _____

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Exhibit A

<first sequence: /home/ruby/va/Molbio/carpenda/ss.incy.2377329 (2377329), length = 197
<second sequence: /home/ruby/va/Molbio/carpenda/ss.DNA68862-2546 (DNA68862-2546), length = 1728

<197 matches in an overlap of 197: 100.00 percent similarity

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                  10        20        30        40        50
2377329H1   GGCCGGACGCCTCCGCGTTACGGGATGAATTAACGGCGGGTTCCGCACGG
            **************************************************
DNA68862    GGCCGGACGCCTCCGCGTTACGGGATGAATTAACGGCGGGTTCCGCACGG
                  10        20        30        40        50

                  60        70        80        90       100
2377329H1   AGGTTGTGACCCCTACGGAGCCCCAGCTTGCCCACGCACCCCACTCGGCG
            **************************************************
DNA68862    AGGTTGTGACCCCTACGGAGCCCCAGCTTGCCCACGCACCCCACTCGGCG
                  60        70        80        90       100

                 110       120       130       140       150
2377329H1   TCGCGCGGCGTGCCCTGCTTGTCACAGGTGGGAGGCTGGAACTATCAGGC
            **************************************************
DNA68862    TCGCGCGGCGTGCCCTGCTTGTCACAGGTGGGAGGCTGGAACTATCAGGC
                 110       120       130       140       150

                 160       170       180       190
2377329H1   TGAAAAACAGAGTGGGTACTCTCTTCTGGGAAGCTGGCAACAAATGG
            ******************************************
DNA68862    TGAAAAACAGAGTGGGTACTCTCTTCTGGGAAGCTGGCAACAAATGGATG
                 160       170       180       190       200

DNA68862    ATGTGATATATGCATTCCAGGGGAAGGGAAATTGTGGTGCTTCTGAACCC
                 210       220       230       240       250

DNA68862    ATGGTCAATTAACGAGGCAGTTTCTAGCTACTGCACGTACTTCATAAAGC
                 260       270       280       290       300

DNA68862    AGGACTCTAAAAGCTTTGGAATCATGGTGTCATGGAAAGGGATTTACTTT
                 310       320       330       340       350

DNA68862    ATACTGACTCTGTTTTGGGGAAGCTTTTTTGGAAGCATTTTCATGCTGAG
                 360       370       380       390       400

DNA68862    TCCCTTTTTACCTTTGATGTTTGTAAACCCATCTTGGTATCGCTGGATCA
                 410       420       430       440       450

DNA68862    ACAACCGCCTTGTGGCAACATGGCTCACCCTACCTGTGGCATTATTGGAG
                 460       470       480       490       500

DNA68862    ACCATGTTTGGTGTAAAAGTGATTATAACTGGGGATGCATTTGTTCCTGG
                 510       520       530       540       550

DNA68862    AGAAAGAAGTGTCATTATCATGAACCATCGGACAAGAATGGACTGGATGT
                 560       570       580       590       600

DNA68862    TCCTGTGGAATTGCCTGATGCGATATAGCTACCTCAGATTGGAGAAAATT
                 610       620       630       640       650

DNA68862    TGCCTCAAAGCGAGTCTCAAAGGTGTTCCTGGATTTGGTTGGGCCATGCA
                 660       670       680       690       700

DNA68862    GGCTGCTGCCTATATCTTCATTCATAGGAAATGGAAGGATGACAAGAGCC
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                  710        720        730        740        750

DNA68862     ATTTCGAAGACATGATTGATTACTTTTGTGATATTCACGAACCACTTCAA
                  760        770        780        790        800

DNA68862     CTCCTCATATTCCCAGAAGGGACTGATCTCACAGAAAACAGCAAGTCTCG
                  810        820        830        840        850

DNA68862     AAGTAATGCATTTGCTGAAAAAAATGGACTTCAGAAATATGAATATGTTT
                  860        870        880        890        900

DNA68862     TACATCCAAGAACTACAGGCTTTACTTTTGTGGTAGACCGTCTAAGAGAA
                  910        920        930        940        950

DNA68862     GGTAAGAACCTTGATGCTGTCCATGATATCACTGTGGCGTATCCTCACAA
                  960        970        980        990       1000

DNA68862     CATTCCTCAATCAGAGAAGCACCTCCTCCAAGGAGACTTTCCCAGGGAAA
                 1010       1020       1030       1040       1050

DNA68862     TCCACTTTCACGTCCACCGGTATCCAATAGACACCCTCCCCACATCCAAG
                 1060       1070       1080       1090       1100

DNA68862     GAGGACCTTCAACTCTGGTGCCACAAACGGTGGGAAGAGAAAGAAGAGAG
                 1110       1120       1130       1140       1150

DNA68862     GCTGCGTTCCTTCTATCAAGGGGAGAAGAATTTTTATTTTACCGGACAGA
                 1160       1170       1180       1190       1200

DNA68862     GTGTCATTCCACCTTGCAAGTCTGAACTCAGGGTCCTTGTGGTCAAATTG
                 1210       1220       1230       1240       1250

DNA68862     CTCTCTATACTGTATTGGACCCTGTTCAGCCCTGCAATGTGCCTACTCAT
                 1260       1270       1280       1290       1300

DNA68862     ATATTTGTACAGTCTTGTTAAGTGGTATTTTATAATCACCATTGTAATCT
                 1310       1320       1330       1340       1350

DNA68862     TTGTGCTGCAAGAGAGAATATTTGGTGGACTGGAGATCATAGAACTTGCA
                 1360       1370       1380       1390       1400

DNA68862     TGTTACCGACTTTTACACAAACAGCCACATTTAAATTCAAAGAAAAATGA
                 1410       1420       1430       1440       1450

DNA68862     GTAAGATTATAAGGTTTGCCATGTGAAAACCTAGAGCATATTTTGGAAAT
                 1460       1470       1480       1490       1500

DNA68862     GTTCTAAACCTTTCTAAGCTCAGATGCATTTTTGCATGACTATGTCGAAT
                 1510       1520       1530       1540       1550

DNA68862     ATTTCTTACTGCCATCATTATTTGTTAAAGATATTTTGCACTTAATTTTG
                 1560       1570       1580       1590       1600

DNA68862     TGGGAAAAATATTGCTACAATTTTTTTTAATCTCTGAATGTAATTTCGAT
                 1610       1620       1630       1640       1650

DNA68862     ACTGTGTACATAGCAGGGAGTGATCGGGGTGAAATAACTTGGGCCAGAAT
                 1660       1670       1680       1690       1700

DNA68862     ATTATTAAACAATCATCAGGCTTTTAAA
                 1710       1720
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